Amendment and Response dated: February 26, 2009

Reply to Office Action of September 30, 2008

In the Claims:

Please amend the claims as follows (the changes in these claims are shown with strikethrough for deleted matter and <u>underlines</u> for added matter). A complete listing of the claims with proper claim identifiers is set forth below.

- 1. (Previously withdrawn) An isolated polypeptide comprising an amino acid sequence having at least 85% sequence identity to SEQ ID NO: 15, 17, or 19, wherein said polypeptide is characterized by high-level expression.
- 2. (Previously withdrawn) The isolated polypeptide of claim 1, wherein said polypeptide comprises an amino acid sequence set forth in SEQ ID NO: 15, 17, or 19.
- 3. (Previously withdrawn) A composition comprising the polypeptide of claim 1.
- 4. (Previously withdrawn) A composition comprising the polypeptide of claim 2.
- 5. (Previously Presented) An isolated nucleic acid molecule encoding a modified factor VIII polypeptide comprising a nucleotide sequence having at least 95% sequence identity to a polynucleotide sequence shown in SEQ ID NO: 18, wherein said nucleotide sequence encodes a polypeptide characterized by high-level expression when compared to a corresponding human factor VIII polypeptide expressed under the same conditions.
- 6. (Previously Presented) The isolated nucleic acid molecule of claim 5, wherein said nucleotide sequence is selected from the group consisting of:
- a) a nucleotide sequence comprising the sequence set forth in SEQ ID NO: 18; and,
- b) a nucleotide sequence comprising the sequence encoding a polypeptide comprising the amino acid sequence at least 95% identical to that set forth in SEQ ID NO: 19.
- 7. (Original) A DNA construct comprising the nucleic acid molecule of claim 5.

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8. (Original) A DNA construct comprising the nucleic acid molecule of claim 6.

- 9. (Original) A vector comprising the nucleic acid molecule of claim 5.
- 10. (Original) A vector comprising the nucleic acid molecule of claim 6.
- 11. (Original) A cell comprising the nucleic acid molecule of claim 5.
- 12. (Original) A cell comprising the nucleic acid molecule of claim 6.
- 13. (Original) A cell comprising the vector of claim 5.
- 14. (Original) A cell comprising the vector of claim 6.
- 15. (Withdrawn) A method of producing a modified factor VIII polypeptide comprising:
- a) introducing into a cell a nucleic acid molecule comprising a nucleotide sequence having at least 95% sequence identity to SEQ ID NO: 18, wherein said sequence encodes said polypeptide and said polypeptide is characterized by high-level expression when compared to a corresponding human factor VIII polypeptide expressed under the same conditions; and
- b) culturing said cell under conditions that allow expression of said nucleotide sequence.
- 16. (Withdrawn) The method of claim 15, wherein said nucleotide sequence is selected from the group consisting of:
- a) a nucleotide sequence comprising the sequence set forth in SEQ ID NO: 18; and,
- b) a nucleotide sequence comprising the sequence encoding a polypeptide comprising the amino acid sequence at least 95% identical to that set forth in SEQ ID NO: 19.
- 17. (Withdrawn) The method of claim 15 further comprising isolating said polypeptide.
- 18. (Withdrawn) The method of claim 16 further comprising isolating said polypeptide.

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19. (Previously withdrawn) A method of increasing the level of expression of a factor VIII polypeptide in a cell comprising:

- a) introducing into said cell a nucleic acid molecule comprising a nucleotide sequence having at least 85% sequence identity to SEQ ID NO: 14, 16, or 18, wherein said sequence encodes said factor VIII polypeptide and said factor VIII polypeptide is characterized by high expression;
- b) culturing said cell under conditions that allow expression of said nucleic acid molecule.
- 20. (Previously withdrawn) The method of claim 19, wherein said nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of:
- a) a nucleotide sequence comprising a sequence encoding a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 15, 17, or 19; and,
- b) a nucleotide sequence comprising the sequence set forth in SEQ ID NO: 14, 16, or 18.
- 21. (Previously withdrawn) The method of claim 19 further comprising isolating said polypeptide.
- 22. (Previously withdrawn) The method of claim 20 further comprising isolating said polypeptide.
- 23. (Previously withdrawn) A method of treating a factor VIII deficiency comprising

administering to a subject in need thereof a composition comprising a therapeutically effective amount of a polypeptide, wherein said polypeptide comprises an amino acid sequence having at least 85% sequence identity to SEQ ID NO: 15, 17, 19 and said polypeptide is characterized by high-level expression.

- 24. (Previously withdrawn) The method of claim 23, wherein said wherein said polypeptide comprises an amino acid sequence set forth in SEQ ID NO: 15, 17, or 19.
- 25. (Previously withdrawn) A method of treating a factor VIII deficiency comprising

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administering to a subject in need thereof a composition comprising a therapeutically effective amount of a nucleic acid molecule, where said nucleic acid molecule comprises a nucleotide sequence having at least 85% sequence identity to SEQ ID NO: 14, 16, or 18, wherein said nucleic acid molecule encodes a factor VIII polypeptide, characterized by high-level expression.

- 26. (Previously withdrawn) The method of claim 25, wherein said nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of:
- a) a nucleotide sequence comprising the sequence set forth in SEQ ID NO: 14, 16, or 18; and,
- b) a nucleotide sequence comprising a sequence encoding a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 15, 17, or 19.

Claims 27-40 (Cancelled).

- 41. (Currently Amended) The isolated nucleic acid molecule of claim 5, wherein the polypeptide further comprises at least one mutation selected from the group consisting of R503A, R508A, P511A, K1155E, T1158A, H116R, E1201D, F1203H, K1220M, K1245R, K1246N, T1249S, S1267A, and I1280V.
- 42. (Currently Amended) The isolated nucleic acid molecule of claim 6, wherein the polypeptide further comprises at least one mutation selected from the group consisting of R503A, R508A, P511A, K1155E, T1158A, H116R, E1201D, F1203H, K1220M, K1245R, K1246N, T1249S, S1267A, and I1280V.
- 43. (Withdrawn and Currently Amended) The method of claim 15, wherein the polypeptide further comprises at least one mutation selected from the group consisting of R503A, R508A, P511A, K1155E, T1158A, H116R, E1201D, F1203H, K1220M, K1245R, K1246N, T1249S, S1267A, and I1280V.